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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,717	02/25/2005	Koji Nagai	Q86534	3693

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EXAMINER	
KOSAR, ANDREW D	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 11/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/525,717	NAGAI ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-6 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-6 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 25 February 2005 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2/25/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-6 are pending and have been examined on the merits.

Information Disclosure Statement

References JP 2001-348340 A and WO 00/42062 A1 have been considered insofar as they are discussed in the specification, their English abstracts and/or corresponding US Patents and PGPub.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 2 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The peptides of formula (I) and (II) are indicated by the specification to be products of nature, as the specification states, "The depsipeptide compound of the present invention be or the pharmaceutically acceptable salt thereof can be obtained by culuring a bacterium producing the compound, which belongs to the genus *Pseudomonas*... As such [species] Q71576, ... isolated from a soil sample... can be used. In order to obviate this rejection, amending the claim to indicate 'hand of man' is required, e.g. 'Isolated', 'purified', etc, such that it is distinguished from that which is produced in nature.

Claim 5 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Specification

The use of the trademark(s), e.g., Amberlite, Diaion, etc. (page 9), has/have been noted in this application. A trademark should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant should capitalize each letter of the word or include a proper trademark symbol, such as ™ or ® following the word. Further, language such as "the product X (a descriptive name) commonly known as Y (trademark)" is impermissible, since such language does not bring out the fact that the latter is a trademark. Language such as "the product X (a descriptive name) sold under the trademark Y" is permissible. See MPEP § 608.01 (v).

Claim Objections

Claims 2 and 4 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 2 recites the physical properties identified in the specification for the peptides of formulae (I) and (II), and does not further limit the claim, as the peptides inherently have the properties identified. Further, claim 4 recites the pharmaceutical composition 'which is an

antitumor agent', which does not further limit the parent claim, as it inherently is an antitumor agent.

Claim 5 is objected to, as it recites 'A method...a method...', and should be amended to recite only one 'A method', i.e.- 'A method for treating a patient...'.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites, "A depsipeptide compound represented by...." It is unclear whether the formulae are the compounds being claimed (e.g. 'An isolated depsipeptide of formula...'), or whether other compounds may be 'represented' by the formulae. As such, the claims are indefinite.

Claim 5 provides for the use of the depsipeptide of claim 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. The claim has been interpreted as a method of making a medicament.

Claim 6 recites, "...a method for treating a patient suffering from cancer...". It is unclear as to what end result the 'treating' is to achieve, and thus the claim is indefinite. For example, it

is unclear whether the method is to treat the cancer in the patient, or whether the method is to treat any condition in a patient who has cancer.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 4 and 5 are rejected under 35 U.S.C. 102(e) as being anticipated by NAGAI (US Patent 6,670,326 B1; PTO-1449, 2/25/2005).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The instant claims are drawn to depsipeptides represented by formulae (I) and (II), a pharmaceutical composition and a method of making. This rejection is predicated on the interpretation that formulae (I) and (II) 'represent' the products being claimed.

Nagai teaches depsipeptides Q and R, which are isolated from the same source, *Pseudomonas* sp. Q71576, according to the instant specification (e.g. pages 6 to 7) and by the prior art and have the same activity, all being antitumor agents. Because they are isolated from the same source and have the same activity, the compounds, absent evidence to the contrary, are the same.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being obvious over NAGAI (US Patent 6,670,326 B1; PTO-1449, 2/25/2005) in view of VOET (D. Voet and J.G. Voet. Biochemistry, 2nd Edition.(1995), page 58).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e).

This rejection under 35 U.S.C. 103(a) might be overcome by:

(1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another";

(2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or

(3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c).

This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The following rejection is predicated on the interpretation that the products are/or can be synthesized *de novo* using standard synthetic techniques.

The instant claims are drawn to depsipeptides of formulae (I) and (II), a pharmaceutical composition, a method of making, and a method of treating a patient suffering from cancer.

Nagai teaches depsipeptides (claim 1) and as a pharmaceutical composition (claim 2) which is an antitumor agent (claim 3). Nagai teaches that "Clinical dose of the compound of the invention in human is optionally decided by taking into consideration symptoms...of each patient to be treated." (column 5, lines 62-65). Nagai teaches that the peptides are "useful as medicaments, particularly as an antitumor agent" (column 1, lines 6-11) and that, "a compound exhibiting TGF-β like activity [such as the compounds of Nagai] has a possibility of becoming therapeutic agents for disease related to said activity, such as antitumor agent." (column 1, line 37-40).

The difference between that which is instantly claimed and that taught by Nagai, is that the compounds of Nagai are S-S bridged, where the instantly claimed compound of formula (I) is S-S-S, and the compound of instant formula (II) is Val/Val, where Nagai is Ala/Val.

The MPEP states, "A prima facie case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and *In re Dillon*, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991)." *See* MPEP § 2144.09.

With regards to formula (II), it would have been obvious to one of skill in the art at the time of the invention to have made the Val/Val compound and use it to treat a patient with cancer, as both compounds have 'very close structural similarities', differing only in the side chain of a single amino acid, which is considered a conservative substitution, as they are both non-polar amino acids (e.g. Voet, page 58), and because they both have 'similar utility', both

functioning as antitumor compounds. With regards to formula (I), it would have been obvious to one of skill in the art to have made the S-S-S bridged compound, as the compounds have 'very close structural similarities', differing only by the interposed sulfur in the Cys-Cys bridge, and because the compounds have 'similar utility', both functioning as antitumor compounds. One would have been motivated to make the Val/Val, or the Cys-Cys bridge with the interposed S, compounds with the expectation that compounds with similar structure would have similar properties, in the instant case, antitumor activity. One would have had a reasonable expectation for success in making the compounds, as peptide synthesis is a routine technique widely practiced in the peptide art.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

NO CLAIMS ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 8am-430pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571)272-0974. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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